REMARKS

In the above amendments, claims 43, 47, 49, 54 and 57-58 have been amended. Claim 43-67 remain in the application.

In the Official Action, restriction was required between the following four groups of claims:

Group I - Claims 43-46, 48, 50-53 and 56, drawn to a viral particle having a modified cell binding activity and a method of making said viral particle comprising the recited steps.

Group II - Claims 43 and 58-67, drawn to a preparation of viral particles incorporating a passenger peptide binding moiety and a method of making said viral particles, said method comprising a step of enriching the titre of said viral particles.

Group III - Claim 49, drawn to a method of treating, preventing or diagnosing a disease or disorder comprising the step of employing a bioactive agent.

Group IV, Claim 57, drawn to a method for preparing an enriched population of a target cell type comprising the recited steps.

It is noted that claims 47, 54 and 55 were not assigned to any of the groups. It is believed that the deficiencies in those claims have been corrected by the above amendments and that they should be assigned to Group I.

In accordance with the restriction/election requirement, applicant elects the claims of Group I containing claims 43-46, 48, 50-53 and 56 (and 47, 54 and 55). This election is made with traverse.

Applicant believes that the claims of Groups I-IV are linked by a single general inventive concept which is generic to all. In the Action, it is the Examiner's view that the technical feature linking Groups I-IV is a viral particle having a modified cell binding activity. However, the applicant believes that, in fact, the novel linking feature of these groups is actually the way in which the binding specificity of the virus is modified and the consequences of that for targeted gene delivery.

The paper cited by the Examiner in support of his position, Cosset et al (Journal of Virology:69:6314-6322, 1995) was contained in applicant's IDS. That paper, indeed, shows a method for redirecting retro viral binding specificity but, applicant submits, that the way in which this is achieved is fundamentally different from the approach of the present invention and the outcome using the present invention is fundamentally different, i.e., through incorporation of a "passenger peptide" and not a modified binding *per se*. A further explanation is offered.

The targeting methodology of the Cossett paper alters binding specificity of the retrovirus by making detailed alterations to the structure of the retroviral envelope protein; the protein by which the virus normally interacts with its target

cells.

There are significant problems with this approach. Manipulating the envelope is unreliable and unpredictable and often leads to poor viral titers. Most commonly, it also renders the virus incapable of infecting target cells. Where infection does occur, it is with extremely low efficiency (much too low for any realistic therapeutic application.

In the Cossett paper, it is noted that the authors concede that their methodology does not result in targeted gene delivery to cells expressing EGFR. The paper acknowledges that most of the binding can be accounted for by the presence of "shed SU", a problem that is not relevant the technology of the present invention.

Moreover, they can only show binding to cells artificially adapted to over-express the targeted protein (EGFR). There is no evidence that this can be achieved with cells that express EGFR at natural levels. The data for the present application was all generated in unmodified target cells.

The present invention avoids manipulation of the envelope protein and instead incorporates molecules expressed on the surface of the cell into the retrovirus as it buds during particle generation. Thus, the virus *per se* is not engineered but instead the cells used to manufacture the virus are modified.

This approach obviates all the problems associated with envelope modification (e.g. poor viral titers). The invention

not only re-directs viral binding, but consequently allows for high efficiency gene delivery specifically to the cells to which the virus binds. One cannot achieve specific gene delivery (to a particular sub-set of cells) without altering binding specificity.

The applications of the technology (claim Group III), it is believed, becomes a logical extension of the method of making the viral particles using the method of the invention (claim Groups I and II). The technology of the prior art, including that of Cossett, is unable to produce results that provide any possible therapeutic application.

Hence, the four claim groups relate to a linked, novel and inventive method of creating viral particles by incorporating peptides from a modified cell surface, as opposed to modifying the particle directly.

In view of the above amendments and the remarks herein, the Examiner is respectfully requested to reconsider and withdraw the present restriction requirement. Early examination and allowance of the claims is respectfully requested.

Respectfully submitted,
NIKOLAI & MERSEREAU, P.A.

C. G. Mersereau
Registration No. 26205
820 International Centre
900 Second Avenue So.
Minneapolis, MN 55402
(612) 339-7461

CERTIFICATE OF MAILING

I hereby certify that the foregoing Amendment in response to the Official Action of April 4, 2006, a Petition for a one-month extension of time, a check in the amount of $120.00 and a Transmittal Letter in application Serial No. 10/520,745, filed on August 22, 2005, of Colin M. Casimir, entitled "METHODS OF MAKING VIRAL PARTICLES HAVING A MODIFIED CELL BINDING ACTIVITY AND USES THEREOF" are being deposited with the U.S. Postal Service as First Class mail in an envelope addressed to Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, postage prepaid, on May 31, 2006.

Barbara L Davis

Barbara L. Davis
on behalf of C. G. Mersereau
Attorney for Applicant

Date of Signature: May 31, 2006